

WHAT IS CLAIMED IS:

- ✓ 1. A method for predicting the binding affinity of a peptide for a MHC protein, comprising providing a prediction of binding affinity by two or more methods, and then combining the predictions of those methods.
2. The method of Claim 1, wherein said MHC protein is a MHC class I protein.
3. The method of Claim 2, wherein said MHC class I protein is an allotype selected from the group consisting of A1, A2, A3, A24, and B7.
4. The method of Claim 1 wherein said peptide is derived from a protein selected from the group consisting of a viral protein and a human protein.
5. The method of Claim 1, wherein the sequence of said peptide is derived from a sequence selected from the group consisting of a sequence from a known protein or a genomic sequence.
6. The method of Claim 1, wherein said combining is performed by a voting method.
7. The method of Claim 1, wherein said predictions of affinity are presented in terms selected from the group consisting of relative binding efficiencies, IC-50 values, and categorical binding affinities.
8. The method of Claim 1, wherein said methods are algorithms selected from the group consisting of quadratic programming, linear programming, and a profile-based method.
9. The method of Claim 8, wherein said profile-based method uses a clustering heuristic selected from the group consisting of iterative multiple alignment, letter frequencies, and position dependencies reflected by (2 tests.
10. The method of Claim 8, wherein said profile-based method employs a principle selected from the group consisting of dimensionality reduction, multiple intra-allelic motifs, and anchor selection.
11. A computer system, comprising programming to perform the method of Claim 1.
12. A computer storage media, comprising programming to perform the method of Claim 1.

13. A method for assigning a categorical binding affinity for a protein to a candidate peptide based on information for a set of known peptides for a protein, comprising:
- obtaining sequence and binding affinity information for a set of known peptides;
 - obtaining sequence data for a candidate peptide;
 - generating an evaluation of the affinity of said candidate peptide for said protein using said sequence and binding affinity information for a set of known peptides and said sequence data for candidate peptides;
 - ranking said candidate peptide and said known peptides on the basis of relative binding affinities for said protein; and
 - assigning peptides to categories of binding affinity based on rank.
14. The method of Claim 13, wherein ranking comprises a list of said known peptides organized by their affinities for said protein.
15. The method of Claim 13, wherein said ranking includes said candidate peptide.
16. The method of Claim 15, wherein said categorical binding affinity of said candidate peptide is expressed as assignment of the peptide to one of two or more classes based on said ranking of said candidate peptide in said list of individual peptides from said set of known peptides.
17. The method of Claim 16, wherein said classes of categorical binding affinity have labels selected from the group consisting of high, medium, low and non-binder.
18. A method for evaluating the affinity of a candidate peptide for a protein, consisting of:
- obtaining sequence and binding affinity information for a set of known peptides;
 - obtaining sequence data for a candidate peptide;
 - generating a first evaluation of affinity of said candidate peptide for said protein by comparing the sequence of said candidate peptide with data developed from said information for a set of known peptides with a first prediction method;
 - generating one or more additional evaluations of affinity of said candidate peptide for said protein using said information for a set of known peptides and one or

more additional prediction methods different from said first method used to generate said first evaluation of affinity; and

combining said first evaluation and said one or more additional evaluations into a combined evaluation.

19. The method of Claim 18, wherein said binding affinity information for a set of known peptides comprises data selected from the group consisting of quantified affinity data for individual peptides in the set, data regarding whether the individual peptides bind said protein or not, data comprising the assignments of known peptides into two or more binding categories, and data that combines two or more of these data types.

20. The method of Claim 19, wherein said data comprising the assignment of known peptides into two or more binding categories comprises assignment of peptides to high, medium, low, and non-binder categories.

21. The method of Claim 18, wherein said prediction method and said one or more additional prediction methods are selected from the group consisting of quadratic programming, linear programming, and a profile-based method.

22. The method of Claim 21, wherein said profile-based method incorporates a method selected from the group consisting of iterative multiple alignment, letter frequencies, and position dependencies reflected by χ^2 tests.

23. The method of Claim 21, wherein one prediction method selected is quadratic programming.

24. The method of Claim 23, wherein a data reduction method, selected from the group consisting of BIMAS-like method and AA-properties method, is used with quadratic programming.

25. The method of Claim 21, wherein said profile-based method implements a principle selected from the group consisting of dimensionality reduction, multiple intra-allelic motifs, and anchor selection.

26. The method of Claim 18, wherein said sequence data for a candidate peptide is selected from the group consisting of data derived from the sequence data of a known protein and data derived from the sequence data of an organism.

27. The method of Claim 18, wherein said sequence data for a candidate peptide is selected from the group consisting of viral protein sequence data and human protein sequence data.

28. The method of Claim 18, wherein said sequence data for a candidate peptide is stored in a centralized database.

29. The method of Claim 18, wherein said sequence and binding affinity information for a set of known peptides is stored in a centralized database.

30. The method of Claim 18, wherein said first evaluation is stored in a centralized database.

31. The method of Claim 18, wherein said one or more additional evaluations is stored in a centralized database.

32. The method of Claim 18, wherein said combined evaluation is stored in a centralized database.

33. The method of Claim 18, wherein said protein is a MHC protein.

34. The method of Claim 33, wherein said MHC protein is a MHC class I protein.

35. The method of Claim 34, wherein said MHC class I protein is an allotype selected from the group consisting of A1, A2, A3, A24, and B7.

36. The method of Claim 18, wherein said combined evaluation comprises assignment of a rank to said candidate peptide based on said candidate peptide's affinity to said protein.

37. The method of Claim 36, wherein said rank based on said candidate peptide's affinity to a protein is a ranking relative to other peptides.

38. The method of Claim 36, wherein said combined evaluation comprises assignment of said candidate peptide to a class, according to said rank based on its affinity to said protein.

39. The method of Claim 18, further comprising the evaluation of additional candidate peptides.

40. The method of Claim 39, further comprising the selection of a subset of candidate peptides based on the combined evaluations of those peptides.

41. A computer system, comprising programming to perform the method of Claim 18.

42. A computer storage media, comprising programming to perform the method of Claim 18.

43. A method for making a vaccine, comprising manufacturing a peptide selected using the method of Claim 18 and preparing a medicament containing the selected peptide.

/ 44. An algorithmic quadratic programming (QP) method, comprising methods for predicting the relative affinities of peptides proteins.

45. The method of Claim 44, further comprising the equation and constraints:

$$\begin{aligned} \min_{w,c} \sum_i (x_i^T w - c - b_i)^2 \\ \text{s.t. } x_{H_i}^T w \geq x_{M_j}^T w \forall i, j, \\ x_{H_i}^T w \geq x_{L_j}^T w \forall i, j, \\ x_{M_i}^T w \geq x_{L_j}^T w \forall i, j, \\ x_{e_i}^T w \geq IC_{\min}^{50}, x_{ne_i}^T w \leq IC_{\min}^{50} \end{aligned}$$

46. The method of Claim 44, further comprising the equation and constraints:

$$\begin{aligned} \min_{w,c} \sum_i (x_i^T w - c - b_i)^2 + \sum_{i,j} e_{H_i M_j}^2 + \sum_{i,j} e_{H_i L_j}^2 + \sum_{i,j} e_{M_i L_j}^2 + \sum_i e_{e_i}^2 + \sum_i e_{ne_i}^2 \\ \text{s.t. } (x_{H_i}^T - x_{M_j}^T)w + e_{H_i M_j} \geq 0 \forall i, j \\ (x_{H_i}^T - x_{L_j}^T)w + e_{H_i L_j} \geq 0 \forall i, j \\ (x_{M_i}^T - x_{L_j}^T)w + e_{M_i L_j} \geq 0 \forall i, j \\ x_{e_i}^T w - IC_{\min}^{50} + e_{e_i} \geq 0 \forall i \\ IC_{\min}^{50} - x_{ne_i}^T w + e_{ne_i} \geq 0 \forall i \end{aligned}$$

/ 47. A linear programming method of predicting peptide affinity for a protein.

48. The method of Claim 47, further comprising the equation and constraint:

$$\begin{aligned} \min \quad & \sum_{aa's} \sum_{a \text{ pos. } p} b_{ap} \\ \text{s.t.} \quad & \sum_{pos. p} b_{e_i^p} \geq 1 \quad \forall i \\ & b_{ap} \geq 0 \quad \forall a, p \end{aligned}$$

/ 49. A profile-based method of predicting peptide affinity for a protein, comprising:

- obtaining information for a set of known peptides;
- creating one or more motifs for peptides with affinity to said protein by analyzing said information for a set of known peptides; and
- evaluating the affinity of a candidate peptide based on said one or more motifs.

50. The method of Claim 49, wherein said information comprises sequence information for said set of known peptides.

51. The method of Claim 49, further comprising a clustering heuristic selected from the group consisting of iterative multiple alignment, letter frequencies, and position dependencies reflected by χ^2 tests.

/ 52. An iterative multiple alignment (*aln*) method of predicting the relative binding affinity of a peptide for a MHC protein, comprising:

- obtaining sequence and affinity information for a set of known epitopes for said MHC protein;
- deriving a motif from said information for a set of known epitopes via an iterative multiple alignment heuristic;
- generating a score for said peptide based on its similarity to said motif; and
- predicting the relative binding affinity of said peptide for said MHC protein based on said score.

53. The method of Claim 52, further comprising:

- deriving multiple motifs from a set of known epitopes via an iterative multiple alignment heuristic;

generating scores for said peptide, each of said scores based on its similarity to one of said motifs; and

predicting the relative binding affinity of said peptide for said MHC protein based on the score showing the highest binding affinity.

54. A letter frequency (LetFq) method of predicting the relative binding affinity of a peptide for a MHC protein, comprising:

obtaining sequence and affinity information for a set of known epitopes for said MHC protein;

deriving a motif from said information for a set of known epitopes via a letter frequency heuristic;

generating a score for said peptide based on its similarity to said motif; and

predicting the relative binding affinity of said peptide for said MHC protein based on said score.

55. The method of 54, further comprising:

deriving multiple motifs from a set of known epitopes via a letter frequency heuristic;

generating scores for said peptide, each of said scores based on its similarity to one of said motifs; and

predicting the relative binding affinity of said peptide for said MHC protein based on the selection of the score showing the highest binding affinity.

56. A method based on χ^2 statistical significance (Ki2) tests predicting the relative binding affinity of a peptide for a MHC protein, comprising:

obtaining sequence and affinity information for a set of known epitopes for said MHC protein;

deriving a motif from said information for a set of known epitopes according to dependencies between peptide positions, revealed by χ^2 significance tests ;

generating a score for said peptide based on its similarity to said motif; and

predicting the relative binding affinity of said peptide for said MHC protein

57. The method of Claim 56, further comprising:

deriving multiple motifs from a set of known epitopes via analysis of position dependencies with χ^2 significance tests

generating scores for said peptide, each of said scores based on its similarity to one of said motifs; and

predicting the relative binding affinity of said peptide for said MHC protein based on the selection of the score showing the highest binding affinity.

58. A method of selecting peptides with a desired level of affinity for a protein, comprising:

obtaining sequence data for a set of candidate peptides and data for peptides of known affinity for said protein; known peptides;

evaluating the affinity of said candidate peptides for said protein using two or more methods, at least one of which uses the data for the peptides of known affinity; and

selecting peptides from said set of candidate peptides that are predicted by said two or more methods to have said desired level of affinity for said protein.

59. The method of Claim 58, wherein said data for peptides of known affinity comprises: a) sequence data and b) data selected from the group consisting of quantitative binding affinity data and qualitative binding data.

60. The method of Claim 58, further comprising using said peptides with a desired level of affinity for a protein for the treatment or prevention of disease.

61. A method for providing treatment for a patient with, or at risk for, cancer or a viral infection, comprising:

obtaining sequence data for candidate peptides;

obtaining data for a set of known peptides;

evaluating the affinity of said candidate peptides for a protein with two or more prediction methods;

selecting candidate peptides with a desired level of affinity for the protein for inclusion in a treatment; and

treating said patient by stimulating an immune response in said patient with said treatment.

62. The method of Claim 61, wherein said sequence data for candidate peptides is selected from the group consisting of sequence data derived from tumor cell proteins,

sequence data derived from tumor cell genes, sequence data derived from viral proteins, and sequence data derived from viral genes.

63. The method of Claim 61, wherein said data for a set of known peptides comprises: a) sequence data and b) data regarding the affinity of said known peptides for said protein.

64. The method of Claim 61, further comprising a step of determining the allotype of said protein, by obtaining genetic information about said patient.

65. The method of Claim 64, wherein said protein is a MHC protein.

66. A method for screening a set of candidate peptides, comprising:
obtaining sequence data for candidate peptides;
obtaining data for a set of known peptides;
evaluating the affinity of said candidate peptides for a protein with two or more prediction methods;
assigning said candidate peptides to two or more groups based on the evaluations of affinity; and
screening said set of candidate peptides on the basis of group assignment.

67. The method of Claim 66, wherein said sequence data for candidate peptides is selected from the group consisting of sequence data of a known protein, sequences of a set of known proteins, and genomic sequences.

68. The method of Claim 67, wherein said sequence data for candidate peptides is generated by dividing the sequence data of a known protein into ninemer or tenmer fragments.

69. The method of Claim 66, wherein said data for a set of known peptides comprises: a) sequence data and b) data regarding the affinity of said known peptides for said protein.

70. A method for identifying epitopes, comprising:
obtaining sequence data for candidate peptides;
obtaining data for a set of known peptide epitopes that bind a MHC protein;
evaluating the affinities of said candidate peptides for said MHC protein using two or more prediction methods and said data for a set of known peptide epitopes;

assigning said candidate peptides to two or more groups based on the evaluations of affinity; and

identifying a set of said candidate peptides by group assignment.

71. The method of Claim 70, wherein said epitopes are T-cell epitopes.

72. The method of Claim 70, wherein said MHC protein is MHC class I protein.

73. The method of Claim 72, wherein said MHC class I protein is an allotype selected from the group consisting of A1, A2, A3, A24, and B7.

74. The method of Claim 70, wherein said two or more prediction methods are selected from the group consisting of quadratic programming, linear programming, and a profile-based method.

75. The method of Claim 74, wherein said profile-based method incorporates a method selected from the group consisting of iterative multiple alignment, letter frequencies, and position dependencies reflected by (2 tests.

76. The method of Claim 74, wherein one prediction method selected is quadratic programming.

77. The method of Claim 76, wherein a data reduction method, selected from the group consisting of BIMAS-like method and AA-properties method, is used with quadratic programming.

78. The method of Claim 70, wherein said evaluations comprise assignment of said candidate peptides and said known peptide epitopes to a rank based on their relative affinity to said MHC protein..

79. A computer system for predicting the affinity of candidate peptides for a protein, comprising:

a database containing data for sets of known peptides;

a database containing sequence information for said candidate peptides;

a processor capable of evaluating peptides by multiple methods; and

a database for storing evaluations.

80. The system of Claim 79, further comprising programming for the execution of said multiple methods of analyzing said candidate peptides.

81. The system of Claim 80, wherein said programming further comprises methods of combining peptide evaluations into a composite evaluation.

82. The system of Claim 79, wherein said evaluations are predictions of affinity of said candidate peptides for a protein.

83. The system of Claim 79, wherein said data for sets of known peptides comprises: a) sequence data and b) data regarding the affinity of said known peptides for a protein.

84. The system of Claim 79, wherein said sets of known peptides comprise peptides that are epitopes with affinity for or recognized by immune system proteins.